CHALLENGES IN CONFORMATIONAL ANALYSIS OF FLEXIBLE MOLECULES

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The conformational analysis represents the first step toward a detailed characterization and understanding of the structure-function relationships of molecular systems. In this respect spectroscopic experiments on isolated bio- and organic-molecules allow detection of different binding schemes and three-dimensional (3D) conformations without perturbing effects of the environment. Detection of multiple 3D-geometries concomitantly present in an experimental mixture can be facilitated by "in situ" structural changes induced either by thermal variations, or the interaction with near-IR (NIR) to ultraviolet (UV) light.

These sophisticated experiments need to be supported by accurate and reliable computational studies allowing to link the rich experimental data to the desired information on the structure and properties of complex molecular systems. Therefore a reliable computational approach should be able to provide a balanced description of all interactions allowing for extended mapping of the whole conformational space, including the accurate prediction of equilibrium structures, their relative positions on the potential energy surface (PES), free energies corresponding to the specific experimental conditions and the spectroscopic properties.

Computations based on the second-order perturbation theory (VPT2) allow accounting for the anharmonicity of both wave function and properties. This results in a correct description of the intensity of non-fundamental transitions and more accurate band-shapes. Moreover, the same anharmonic force fields as employed in the determination of vibrational spectra allow considering vibrational corrections to molecular properties or thermodynamic functions. For flexible molecules, the large amplitude-motion (LAM) free approach, where all LAMs anharmonic constants are excluded, allows overcoming problems due to contaminating the overall VPT2 treatment and higher frequency vibrations.

The most reliable structural, spectroscopic and energetic results can be obtained combining various computational methods ranging from density functional theory (DFT) to coupled-cluster (CC), with the latter representing also references for the benchmarking of different DFT methodologies.